

## Is the WHO analgesic ladder still valid?

### *Twenty-four years of experience*

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Pain remains one of the main reasons for medical consultation worldwide. Numerous organizations and scientific associations have made efforts to find solutions for this problem and to facilitate the treatment of pain. In 1986 the World Health Organization (WHO) presented the analgesic ladder as a framework that physicians could use when developing treatment plans for cancer pain. This therapeutic guideline paved the way for considerable improvements in the management of cancer pain, but is it still a valid tool 24 years later?

The WHO proposed the analgesic ladder following the recommendations of an international group of experts. The document was translated into 22 different languages and has served as a catalyst for increasing awareness around the world of the importance of treating pain in cancer patients.<sup>1-6</sup> The analgesic ladder proposed the use of a limited number of relatively inexpensive medications, such as morphine, in a step-wise approach. It helped legitimize the use of opioids for treatment of cancer pain and encouraged numerous worldwide teaching campaigns on the use, benefits, and side effects of narcotics in the treatment of pain.

Both the 1986 and 1997<sup>1,2</sup> WHO treatment guides for cancer pain provide explanations of the pathophysiology of such pain, how to make adequate assessments, how to choose analgesics, and how to use the ladder. Early studies on its effectiveness demonstrated that the method proposed by the WHO offered inexpensive treatment and adequate relief for 70% to 90% of cancer patients with pain.<sup>2</sup> Today this percentage has been questioned, and the range is now thought to be 70% to 80%.<sup>7,8</sup>

### Simple advice still relevant

The cornerstone of the WHO document rests on 5 simple recommendations for the correct use of analgesics to make the prescribed treatments effective. This advice is applicable today, not only for cancer patients with pain, but also for all patients with either acute or chronic pain who require analgesics.<sup>2</sup> The 5 points for the correct use of analgesics are as follows:

**1. Oral administration of analgesics.** The oral form of medication should be privileged whenever possible.

**2. Analgesics should be given at regular intervals.** To relieve pain adequately, it is necessary to respect the duration of the medication's efficacy and to prescribe the dosage to be taken at definite intervals in accordance with the patient's level of pain. The dosage of medication should be adjusted until the patient is comfortable.

**3. Analgesics should be prescribed according to pain intensity as evaluated by a scale of intensity of pain.** This point is important because pain-relief medications should be prescribed after clinical examination and adequate assessment of the pain. The prescription must be given according to the level of the patient's pain and not according to the medical staff's perception of the pain. If the patient says that he has pain, it is important to believe him. This point makes reference to the levels of the analgesic ladder that will be explained in detail further below.

**4. Dosing of pain medication should be adapted to the individual.** There is no standardized dosage in the treatment of pain. Every patient will respond differently. The correct dosage is one that will allow adequate relief of pain. The posology should be adapted to achieve the best balance between the analgesic effect and the side effects.

**5. Analgesics should be prescribed with a constant concern for detail.** The regularity of analgesic administration is crucial for the adequate treatment of pain. Once the distribution of medication over a day is established, it is ideal to provide a written personal program to the patient. In this way the patient, his family, and medical staff will all have the necessary information about when and how to administer the medications.

The 1986 version of the WHO analgesic ladder proposes that treatment of pain should begin with a nonopioid medication (**Figure 1**).<sup>1</sup> If the pain is not properly controlled, one should then introduce a weak opioid. If the use of this medication is insufficient to treat the pain, one can begin a more powerful opioid. One should never use 2 products belonging to the same category simultaneously.<sup>1,2</sup> The analgesic ladder also includes the possibility of adding adjuvant treatments for neuropathic pain or for symptoms associated with cancer.

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This diagram, which is very simple and clear, has been the object of numerous debates and criticisms,<sup>6,9,10</sup> owing in part to omissions as well as to the development of new techniques and medications.<sup>9,11-13</sup>

## Adapting the ladder

Several proposed modifications of the WHO diagram have been made; one of them even proposes the elimination of the second level.<sup>5,10</sup> Others recommend modifications and adaptations of the analgesic scale for other types of pain, such as acute pain and chronic noncancer pain.<sup>8,12,14,15</sup>

Despite the debate and updates to the 1986 analgesic diagram, its educational value and the benefits resulting from its worldwide dissemination are uncontested. However, the extension of its use to other types of pain has run into some roadblocks.<sup>9,16</sup> Some believe that beginning step by step is often insufficient and inefficient for controlling intense pain,<sup>16</sup> and therefore a fast-track diagram has been proposed starting directly at step 3.<sup>15-17</sup>

The adaptation of the analgesic ladder for acute pain, chronic noncancer pain, and cancer pain offered here (Figure 2) is based on the same principles as the original ladder. This revision integrates a fourth step and includes consideration of neurosurgical procedures such as brain stimulators.<sup>14,15,17</sup> Invasive techniques, such as nerve blocks and neurolysis (eg, phenolization, alcoholization, thermocoagulation, and radiofrequency<sup>6,15,16</sup>), are used at the fourth step. This adapted model has also been proposed and applied in the treatment of pediatric pain,<sup>18,19</sup> and it can be used for acute pain in emergency departments and in postoperative situations.

The new fourth step is recommended for the treatment of crises of chronic pain. Interventional pain literature suggests that there is moderate evidence for

the use of transforaminal epidural steroid injections, lumbar percutaneous adhesiolysis, and spinal endoscopy for painful lumbar radiculopathy, and limited evidence for intradiscal treatments in low back pain.<sup>20</sup> Medullar and peripheral stimulators also have been included at the fourth level.

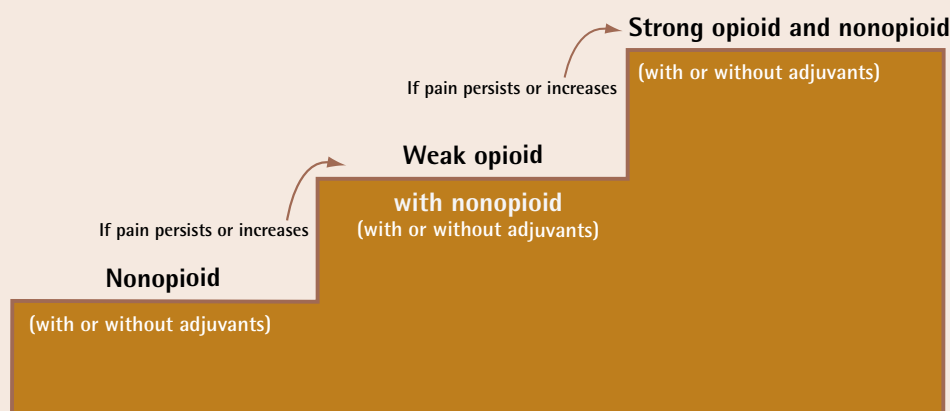
**Opioids.** This new adaptation of the analgesic ladder adds new opioids,<sup>14,15,21-26</sup> such as tramadol, oxycodone, hydromorphone, and buprenorphine, and also new ways of administering them, such as by transdermal patch, that did not exist in 1986. Opioids are classified as weak or strong, as this classification is used in daily practice by millions of physicians throughout the world with excellent results.

The use of opioids to treat chronic noncancer pain is founded on the information gleaned after the first 10 years of dissemination and worldwide use of the analgesic ladder. Since the 1990s, numerous medical articles have been published promoting opioids as a safe treatment for patients with chronic noncancer pain.<sup>20-23</sup>

Methadone, in step 3, is important because it is currently very useful in the treatment of cancer pain, chronic noncancer pain, and refractory neuropathic pain that does not respond to conventional treatment.<sup>15,24,25</sup> Methadone is also very useful in the rotation of opioids<sup>15,21-27</sup> in cancer pain.

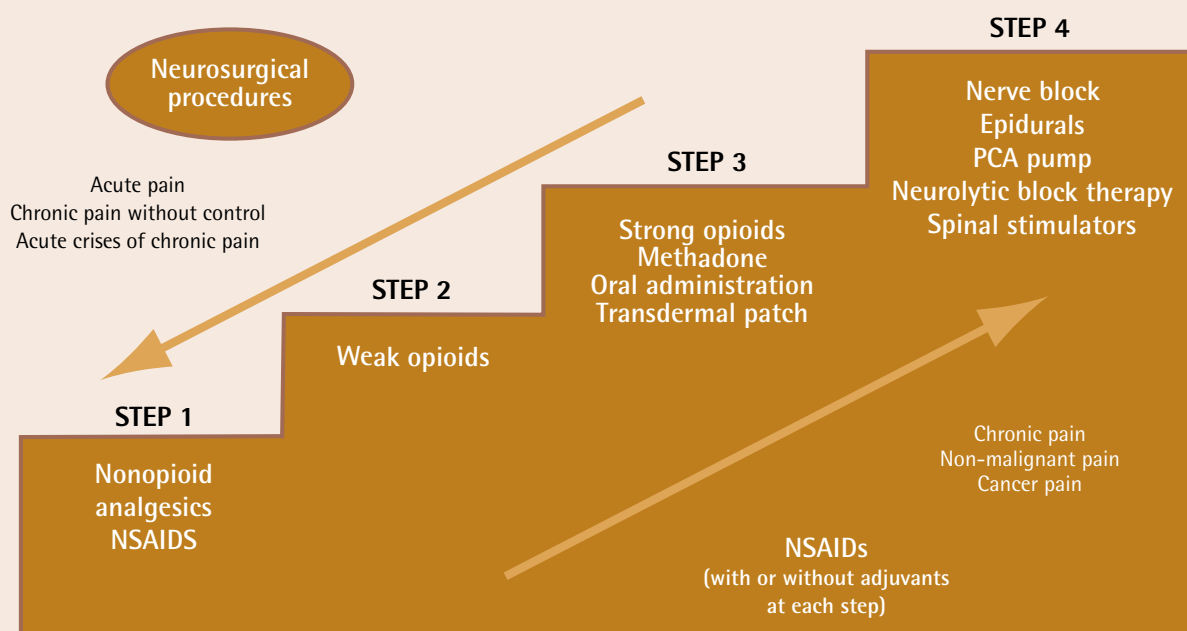
**Adjuvants.** Adjuvant medications include steroids, anxiolytics, antidepressants, hypnotics, anticonvulsants, antiepileptic-like gabapentinoids (gabapentin and pregabalin), membrane stabilizers, sodium channel blockers, and *N*-methyl-D-aspartate receptor antagonists for the treatment of neuropathic pain. Cannabinoids can be added to this group of adjuvant medications, not only because they hold a place as

Figure 1. The World Health Organization analgesic ladder for treating cancer pain



Adapted from the World Health Organization.<sup>1</sup>

**Figure 2. New adaptation of the analgesic ladder**



NSAID—nonsteroidal anti-inflammatory drug, PCA—patient-controlled analgesia.

adjuvants in the care of palliative cancer patients and patients affected by AIDS, but also because they can be used to offer a better quality of life to patients with chronic pain. They can also be used to treat chronic neuropathic pain.<sup>28-35</sup>

**Step up, step down.** This version of the analgesic ladder can be used in a bidirectional fashion: the slower upward pathway for chronic pain and cancer pain, and the faster downward direction for intense acute pain, uncontrolled chronic pain, and breakthrough pain. The advantage of this proposal is that one can ascend slowly one step at a time in the case of chronic pain and, if necessary, increase the rate of climb according to the intensity of the pain. However, one can start directly at the fourth step, in extreme cases, to control pain of high intensity, using patient-controlled analgesia pumps for continuous intravenous, epidural, or subdural administration. When the pain is controlled, one can “step down” to medications from step 3.

**Pure neuropathic pain.** This adaptation can be used for nociceptive pain and for combined nociceptive and neuropathic pain, but not for pure neuropathic pain. In neuropathic pain the treatment algorithm is completely different, and opioids should be considered adjuvant medications and not the principal drugs for the treatment of such pain. Two practice guidelines for the

treatment of neuropathic pain were published in 2007, the first by the Canadian Pain Society<sup>35</sup> and the second by the International Association for the Study of Pain.<sup>34</sup>

## Conclusion

This proposed modification of the WHO analgesic ladder is not intended to negate or advise against use of the original ladder. On the contrary, after 24 years of use the analgesic ladder has demonstrated its effectiveness and widespread usefulness; however, modifications are necessary to ensure its continued use for knowledge transfer in pain management.

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### Competing interests

None declared

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